

AMENDMENTS TO THE DRAWINGS:

The attached sheets of drawings include replacement sheets 1-5, and new sheets 6-12. The replacement sheets change the page numbers only from 1/5 - 5/5 to 1/12 - 5/12. The new sheets add new drawing Figures 6-12.

Attachment: Replacement Sheets and New Drawing Figures

REMARKS

I. CLAIM STATUS

Claims 17-32 were pending when last examined. Claim 25 is canceled, claims 17-19, 21, 23 and 24 are amended, and new claim 33 is added. Claims 22 and 26-32 have been withdrawn from consideration. Upon entry of this amendment, claims 17-24 and 26-33 will be pending.

The specification has been amended and new drawings sheets provided. The amended specification removes chemical reaction schemes and references the reaction schemes in the Figures. The new drawings illustrate the reaction schemes. The amended specification also references new Figures 6-12 in the Description of the Figures. No new matter has been added.

Support for the new and amended claims can be found in the specification and the original claims as filed. No new matter has been added. A clean copy of the claims incorporating the amendments is included in the Appendix.

II. ALLOWABLE SUBJECT MATTER

Applicants gratefully acknowledge the indication, at page 3 of the Office Action, that claim 23 contains allowable subject matter and that additional subject matter is found to be free of the prior art.

III. OBJECTIONS TO SPECIFICATION

At pages 3-4, the Office Action objects to the specification as not in compliance 37 C.F.R. §1.58(a). The Office Action objects to the specification for containing chemical synthesis schemes. Applicants respectfully traverse the objection.

Applicants submit herein a substitute specification, and new drawing sheets with new Figures 6-12. The substitute specification removes the chemical synthesis reaction diagrams, and the reaction diagrams are now shown in Figures 6-12. Accordingly, Applicants request reconsideration and withdrawal of the objection to the specification.

IV. CLAIM OBJECTIONS

At page 4, the Office Action objects to claims 18 and 19 because of informalities. Applicants respectfully traverse the objection.

Currently amended claims 18 and 19 address the informalities noted in the Office Action. Amended claim 18 further clarifies the peptides. Amended claim 19 removes superscript numbers. Applicants request reconsideration and withdrawal of the claim objection.

V. CLAIM REJECTIONS - 35 USC § 112, FIRST PARAGRAPH

Written Description

At page 5, the Office Action rejects claims 17-21, 24 and 25 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Office Action holds the position that the specification and the examples included therein do not sufficiently support the breadth of the claims. Currently amended claim 17 is directed in part to a multimeric molecule of general formula $A-X_n$, wherein A is a chemical moiety, and X represents a -D, -B -D, or -B(D)-D' group, in which B is a spacer arm and -D and -D' each represent a peptide corresponding to a sequence derived from a ligand, said ligand being CD40L. The Office Action acknowledges that the specification supports CD40 receptor ligands.

The Office Action further contends that the specification does not support "pseudopeptides." In currently amended claim 17, -D and -D' no longer include "pseudopeptides."

In addition, because claim 17 features D and D' groups representing a peptide corresponding to a sequence derived from a ligand (CD40L), randomly selected peptides would be unable to interact with a given receptor. As recited in claim 17, peptides D and D' each represent a peptide of a ligand of CD40 receptor, therefore, *a priori*, they are able to interact with the receptor.

The Office Action also takes issue with the examples of a "spacer arm" described in the specification. The "spacer arm" is defined in the specification as "an organic chain used to move the D group to the desired distance from A." The spacer arm does not interact with the receptor, and does not provide any multimeric structure to the compound. The purpose of the spacer arm is to reduce the steric hindrance between groups A and D (and D'). Furthermore, the specification discloses an ϵ -amino acid linker. One of ordinary skill in the art would recognize that the exact nature of the organic chain used as a spacer is not relevant because it is the spacing of groups A and D that is important. Multiple examples of a spacer arm are not required to be shown.

The Office Action also takes issue with the "core molecule" described in the specification. The specification defines group A as a "core molecule" and a "chemical group having a central role in the presentation of the nX groups in the multimeric molecule." The core molecule does not interact with the receptor. The purpose of the core is to provide nX groups, i.e., to create the multiplicity of the claimed compounds.

The Office Action acknowledges that the specification describes at least 13 species of the core molecule A. Furthermore, 35 U.S.C. § 112 does not require a description of all the variations which might suggest themselves to one of ordinary skill in the art. One of ordinary skill would recognize that the exact nature

of the core molecule is relevant only to the extent of obtaining the required multiplicity of the compound.

For all of these reasons, the specification provides written description support for each of claims 17-21 and 24, as currently amended, and each of the claims satisfies the requirements of 35 U.S.C. § 112, first paragraph. Thus, Applicants request reconsideration and withdrawal of this aspect of the rejection.

Enablement

At page 9, the Office Action rejects claim 25 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Claim 25 is canceled, thus rendering moot this rejection. Applicants request reconsideration and withdrawal of this aspect of the rejection.

VI. CLAIM REJECTIONS - 35 USC § 112, SECOND PARAGRAPH

At page 11, the Office Action rejects claims 17-21 and 23-25 under 35 U.S.C. § 112, second paragraph as being indefinite. Applicants respectfully traverse this rejection.

Currently amended claim 17 recites that -D and -D' each represent a peptide.

Currently amended claims 17 and 19 no longer recite the "in particular" statements.

Currently amended claim 17 recites that A is a "chemical moiety."

Currently amended claim 19 further clarifies that the "fragments" refer to "said peptides and hybrid peptides."

Currently amended claim 21 corrects the C₃ symmetry of compounds VIb and VIc.

Currently amended claim 23 similarly corrects the symmetry to the VIb and VIc core in the 5th and 6th compounds.

Regarding claims 21 and 23, the Office Action considers that the term "a chemical group" (claim 17) does not provide antecedent basis to the "macromolecules" described in claims 21 and 23. Currently amended claim 17 recites A is a "chemical moiety" as suggested in the Office Action. The term "chemical moiety" does not induce a preconceived idea about the size of the chemical group. Atoms, molecules, and macromolecules can all be considered moieties. Thus, "macromolecules" in claims 21 and 23 does not lack antecedent basis.

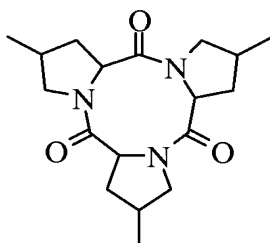
Currently amended claim 23 features "peptide sequence KGYG disclosed as SEQ ID NO: 3" and no longer features peptide sequence YYGK and SEQ ID NO: 4.

Currently amended claim 24 is directed to a pharmaceutical composition that includes a pharmaceutically acceptable "carrier" as recommended in the Office Action.

VII. CLAIM REJECTIONS - 35 USC § 102

At page 14, the Office Action rejects claims 17, 20, 21, 24 and 25 under 35 U.S.C. § 102(b) as anticipated by ROSENBERG (WO 99/52877 A1). Applicants respectfully traverse the rejection.

The Office Action holds the position that ROSENBERG teaches a trimeric C_3 symmetry core structure of the following formula:



to which ligands are bound, and that the claimed compounds are trimeric. The Office Action further considers that ROSENBERG identifies TNF receptor as trimeric, and teaches a core structure that can be of the formula $Q-[R_n-Z]_3$ where Q is nitrogen. Applicants respectfully disagree with this position.

First, ROSENBERG teaches that CD40 is a dimeric receptor:

"Known multimeric homodimerizing receptors include [...] CD40 receptor and CD27 receptor" (page 3, lines 27-35).

"The method of claim 2 wherein the dimeric receptor is [...] CD40 receptor or CD27 receptor" (claim 8, page 19).

Furthermore, claim 2 in ROSENBERG also teaches that the receptor according to claim 1 is a dimeric receptor (claim 2, page 19), and claim 1 teaches *"A method for agonizing or*

antagonizing a multimeric receptor comprising contacting the multimeric receptor with a non-antibody multimeric receptor ligand." (claim 1, page 19).

ROSENBERG further teaches: *"Most preferably, the spacer will provide spatial separation and steric orientation of the binding moieties which mimic the binding moieties of the natural ligand."* (page 4, lines 13-16). Thus, ROSENBERG teaches a method for antagonizing a dimeric receptor (CD40) with a non-antibody dimeric ligand.

Furthermore, ROSENBERG provides examples of the synthesis of only disubstituted spacers and fails to teach the synthesis of any trisubstituted spacer.

Thus, ROSENBERG teaches that CD40 ligands are dimeric, and teaches away from ligands that are known to be trimeric.

Second, ROSENBERG fails to teach the isolation or characterization of a CD40 ligand, and fails to teach the structure of a CD40 ligand, or any other ligand. Critically, ROSENBERG also fails to teach the structure or synthesis of a trimeric compound. As a result, ROSENBERG fails to enable one of ordinary skill in the art to make or use trimeric compounds, and thus, cannot serve as a prior art reference.

As recently repeated by the Federal Circuit, the law of anticipation *"requires the specific description as well as enablement of the subject matter at issue. To anticipate, the reference must not only disclose all elements of the claim within*

the four corners of the document, but also disclose those elements 'arranged as in the claim'." (Sanofi-Synthelabo v. Apotex, CAFC, December 12, 2008).

For all of these reasons, ROSENBERG fails to teach or suggest, and fails to anticipate, a multimeric molecule having all of the features as recited in claim 17, and claims 18, 20, 21 and 24 dependent thereon. Claim 25 is canceled. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

VIII. DOUBLE PATENTING

At page 15, the Office Action provisionally rejects claims 17-21, 24 and 25 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 11/721,910. Applicants respectfully traverse the rejection.

The claims of the '910 application are drawn to compounds containing ligands (Rc) that contain non-natural amino acids. Claims 13 and 14 of the '910 application, for example, describe compounds containing at least two non-natural amino acids.

In contrast, instant claims 17-24 are drawn to peptides (D and D') corresponding to sequences derived from receptor ligands, thus, the peptides contain only natural amino acids, i.e., the natural amino acids of CD40. Claims 17-21 and 24 are

patentably distinct from the compounds and compositions recited in claims 1-20 of copending Application No. 11/721,910. Claim 25 has been canceled. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

IX. CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following items:

- ☒ - Replacement Sheets for pages 1-5 and new drawing sheets for Figures 6-12
- ☒ - a Substitute Specification and a marked-up copy of the originally-filed specification
- ☒ - a clean copy of the claims as amended.